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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	[illegible]
09/715,294	11/17/2000	Narendra S Yadav	CL1127 US CIP	[illegible]

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4417 LANCASTER PIKE
WILMINGTON, DE 19805

EXAMINER

[illegible]

DATE MAILED: [illegible]

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/715,294	YADAV, NARENDRA S.	
	Examiner	Art Unit	
	Ashwin Mehta	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2002* .

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-43,70 and 80-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-43,70 and 80-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01/13/2003 & 02/03/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)[ ] The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

However, see Page 2.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. The objection to claim 38 is withdrawn in light of its cancellation.

3. The rejections of claims 36-43 under 35 U.S.C. 112, 2nd paragraph, are withdrawn in light of the claim amendments or cancellations.

Priority

4. In the paper received 23 December 2002, Applicants revised the priority statement on page 1 of the specification to indicate that the instant application is a CIP of 09/442.021, filed 17 November 1999, which claims the benefit of U.S. Provisional Application 60/063,504, filed 24 October 1997. However, as 09/442,021 was filed more than one year after the filing date of 60/063,504, the instant application cannot claim the benefit of the provisional application.

Information Disclosure Statement

5. An IDS was received on 25 November 20002, accompanied by a single reference. However, a Form 1449 was not submitted. The reference has been considered, and is cited in the accompanying Notice of References Cited.

Claim Objections

6. Claim 39 is objected to because of the following informalities: In the second line of part 2)a), a typographical error appears in the recitation "elementsand". Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. Claims 42 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 42 and 43 are dependent on cancelled claims 36 and 37, respectively.

8. Claims 82, 84, and 86 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for conditionally activating a transgene in a second generation plant when the promoter of the third recombinase element is not active in the common germline, does not reasonably provide enablement for the claimed methods when the promoter of the third recombinase element is active in the common germline. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record stated in the Office action mailed 15 July 2002 under item 7 for claims 36-38 and 43. Applicant traverses the rejection in the paper received 23 December 2002. Applicant's arguments have been fully considered but were not found persuasive.

Applicants argue that in new claims 82, 84, and 86, the P1 and P2 promoters are both active in the common germline, with P2 being active concomitantly with or after P2, and that P3 may be a germline promoter, but that it will only become active in the second generation plant and not in the first generation germline cells (response, page 14, 2nd full paragraph). Applicants argue that support for the new claims can be found in the specification, and recite those passages from the specification (response, paragraph bridging pages 14-15 to page 15, 1st full paragraph).

However, Applicants do not provide any examples of promoters that may be active in germline cells, but which would somehow discriminate the germline cells of a first generation plant from those of a second generation plant. As the recombinase that excises the stop fragment, that separates the P3 promoter from the TG, is active in the germline cells in a first generation plant, P3 would become operatively linked to the TG within the germline cells in the first generation plant. If P3 is active in germline cells, it will direct transcription of TG in the germline cells of the first generation plant. It is not clear, and is not taught in the specification, including in the passages pointed out by Applicants, why a P3 promoter that is active in germline cells would be in active in the germline cells of the first generation plant of the claimed methods. See Genentech, Inc. V. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Claim Rejections - 35 USC § 103

9. Claims 39-41, 70, and 80 remain and claims 81-86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Odell et al. "A" (Mol. Gen. Genet., 1990, Vol., 223, pages 369-378) in

combination with Lloyd et al. (Mol. Gen. Genet., 1994, Vol. 242, pages 653-657), Applicant's admitted state of the prior art , and Odell et al. "B" (Use of Site-Specific Recombination Systems in Plants, in Homologous Recombination and Gene Silencing in Plants, 1994, pages 219-270, Ed. Paszkowski, J., Publisher: Kluwer, Dordrecht, Germany), for the reasons of record stated in the Office action mailed 15 July 2002 under item 8 for claims 36-43, 70, and 80. Applicant traverses the rejection in the paper received 23 December 2002. Applicant's arguments have been fully considered but were not found persuasive.

Applicants argue that there was no reasonable expectation of success in obtaining the present invention. Applicants argue that Odell et al. A and Lloyd et al. teach only single site-specific recombination, do not teach combinations of two or more site-specific recombinase elements, and do not suggest combining more than one site-specific recombinase element to control the timing of expression of a transgene in a plant (response, page 17, 2nd full paragraph). However, Odell et al. A and Lloyd et al. demonstrate that more than one site-specific recombinase system is active in plants. Odell et al. B also assert that the ability of site-specific recombinases to locate their target sites on individual chromosomes is quite impressive (page 260). Given these teachings, one of ordinary skill in the art had a reasonable expectation of success that two different site-specific recombination systems can work in the same plant without interfering with each other.

Applicants also argue that the cited references do not suggest the novel applications that result by introduction of multiple site-specific recombinase elements into a plant, and thus the skilled person would haven no reasonable expectation of success in deriving the present invention from the teaching in the art (response, paragraph bridging pages 17-18). However, as

it was known in the art that different site-specific recombination systems were active in plants, there was no reason to believe that two different systems would suddenly become inactive when used simultaneously in the same plant, nor do Applicants present evidence of any such "problems" in the art. Applicants also argue that while single site-specific recombinase elements can serve to turn genes 'ON' or 'OFF' (transgene removal), linked site-specific recombination can serve as either an 'ON-OFF' or 'ON-ON' switch (response, paragraph bridging pages 17-18). However, this argument is not commensurate with the scope of the claims. The claims of the instant invention do not encompass turning transgenes 'OFF.' See *In re Lindner*, 173 USPQ 356 (CCPA 1972) and *In re Grasselli*, 218 USPQ 769 (Fed. Cir. 1983) which teach that the evidence of nonobviousness should be commensurate with the scope of the claims. Further, Odell et al. B assert that the versatility, efficiency, and specificity of site-specific recombination systems allow their use in a wide range of uses and applications (page 260). It is not necessary that a reference actually suggest changes that Applicant made. See *In re Scheckler*, 438, F.2d 999, 1001; 168 USPQ 716, 717 (CCPA 1971). Modifications can be derived from an analysis of the prior art without a specific statement in the reference. See *In re Bozek* (416 F.2d 1385, 1390, 163 USPQ 545, 549 (CCPA 1969)), which teaches, "having established that this knowledge was in the art, the examiner could then properly rely...on a conclusion of obviousness 'from common knowledge and common sense of the person of ordinary skill in the art without any specific hint or suggestion in a particular reference'."

Applicants also argue that, at best, the skilled person might find it obvious to try to use two or more site-specific recombinase elements (response, paragraph bridging pages 17-18). However, given that the specificity, efficiency, and versatility of different site-specific

recombination systems in plants was known in the prior art, as discussed above, Applicants have not presented any evidence that different systems would be inactive when used in the same plant. Note that it also would have been obvious for one of ordinary skill in the art to use a common germline promoter as P3, when transgene expression in the germline of the first generation plant was desired. Any plant promoter could have been chosen as P3, and depended on one's desired end. The rejection is withdrawn from claims 42 and 43 as they are now dependent on cancelled claims.

Summary

10. Claims 39-43, 70, and 80 remain and claims 81-86 are rejected.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this or earlier communications from the examiner should be directed to Ashwin Mehta, whose telephone number is 703-306-4540. The examiner can normally be reached on Mondays-Thursdays and alternate Fridays from 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 and 703-872-9306 for regular communications and 703-872-9307 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

April 2, 2003

ASHWIN D. MEHTA, PH.D
PATENT EXAMINER